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Preventing a first episode of psychosis: Meta-analysis of randomized controlled prevention trials of 12 month and longer-term follow-ups

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ABSTRACT

Over the last decade many studies were conducted to assess the feasibility of early detection of people at risk of developing psychosis and intervention to prevent or delay a first psychotic episode. Most of these studies were small and underpowered. A meta-analysis can demonstrate the effectiveness of the efforts to prevent or postpone a first episode of psychosis.

A search conducted according the PRISMA guideline identified 10 studies reporting 12-month follow-up data on transition to psychosis, and 5 studies with follow-ups varying from 24 to 48 months. Both random and fixed effects meta-analyses were conducted.

The quality of the studies varied from poor to excellent. Overall the risk reduction at 12 months was 54% (RR = 0.463; 95% CI = 0.33–0.64) with a Number Needed to Treat (NNT) of 9 (95% CI = 6–15). Although the interventions differed, there was only mild heterogeneity and publication bias was small. All sub-analyses demonstrated effectiveness. Also 24 to 48-month follow-ups were associated with a risk reduction of 37% (RR = .635; 95% CI = 0.44–0.92) and a NNT of 12 (95% CI = 7–59). Sensitivity analysis excluding the methodologically weakest study showed that the findings were robust.

Early detection and intervention in people at ultra-high risk of developing psychosis can be successful to prevent or delay a first psychosis. Antipsychotic medication showed efficacy, but more trials are needed. Omega-3 fatty acid needs replication. Integrated psychological interventions need replication with more methodologically sound studies. The findings regarding CBT appear robust, but the 95% confidence interval is still wide.

1. Introduction

The identification of individuals at high risk of developing a psychotic disorder has long been a goal of clinicians because it is thought that early treatment of this group may prevent onset of the disorder, or at least minimize its impact. Over the last 20 years, two broad sets of criteria have been used to diagnose the Clinical High Risk (CHR) state: the Ultra High Risk (UHR) and the Basic Symptoms (BS) criteria. The UHR state requires the presence of one or more of: attenuated psychotic symptoms (APS), brief limited intermittent psychotic symptoms (BLIPS), or trait vulnerability plus a marked decline in psychosocial functioning (Genetic Risk and Deterioration Syndrome: GRD). BS are subjectively experienced disturbances of different domains including perception, thought processing, language and attention that are distinct from classical psychotic symptoms, in that they are independent of abnormal thought content, reality testing and insight into the symptoms' psychopathological nature. Reliable and valid instruments have been developed and refined to identify the UHR group (Miller et al., 2002; Yung et al., 2005) and the BS group (Schutze-Lutter et al., 2007). CHR subjects who met UHR or BS criteria or a combination of both had a transition rate of 18% after 6 months, 22% after one year, 29% after two years and 36% after three years (Fusar-Poli et al., 2012).

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The first prevention trials were small. A meta-analysis was conducted using the data from the first five randomized controlled trials (Preti and Cella, 2010). The pooled relative risk was 0.36, meaning that the risk of a first psychosis was reduced by 64%, and statistically significant. Heterogeneity was absent, meaning that differences across the primary studies could be attributed to random sample error rather than to systematic factors. The Cochrane group conducted another meta-analysis using six studies, but did not pool the data (Marshall and Rathbone, 2011). The most recent meta-analysis was based on seven studies (Fusar-Poli et al., 2013) and reported a relative risk of 0.34 (95% CI: 23–7; $p < 0.001$), indicating the interventions were successful in reducing the risk of a first psychotic episode in a statistically significant way by 66%. These outcomes were associated with a number needed to treat (NNT) of 6 indicating that 6 UHR individuals need to receive treatment for preventing one more transition to psychosis compared to treatment as usual.

Currently, a total of ten prevention trials in CHR have been conducted doubling the number of trial participants and thus strengthening the evidence-base considerably. The aim of the present study is to conduct a meta-analysis of the ten prevention trials in CHR to obtain a more precise understanding of the feasibility to prevent the transition from a high-risk status to a psychotic episode.

2. Methods

2.1. Data collection

Only randomized controlled trials were included. Any control condition was accepted.

We conducted literature searches following the PRISMA guideline (Liberati et al., 2009) using five databases: Ovid MEDLINE and EMBASE, both from 1996 to November 2012, PsycINFO from 1987 to November 2012, EBM Reviews — Cochrane Central Register of Controlled Trials, and EBM Reviews — Cochrane Database of Systematic Reviews, 2005 to November 2012. We also examined published reviews and meta-analyses. Within each of the databases three searches were carried out:

The first search was on “prodromal” (7201), “ultra-high risk” (1099) OR “ultra high risk” (61) OR “high clinical risk” (188) OR “clinical high risk” (417) OR “at risk mental state” (509) OR “risk of progression” (7055) OR “progression to first-episode psychosis” (9) OR “prodromally symptomatic” (28);

The second search was on “RCT” (20,968) OR "randomised controlled trial" (19,886) OR "randomized controlled trial" (560,250);

The third search was on “psychosis” (90,442)

Combining the three searches and the examination of the reviews resulted in 118 references (see Fig. 1). Removing duplicates left 70

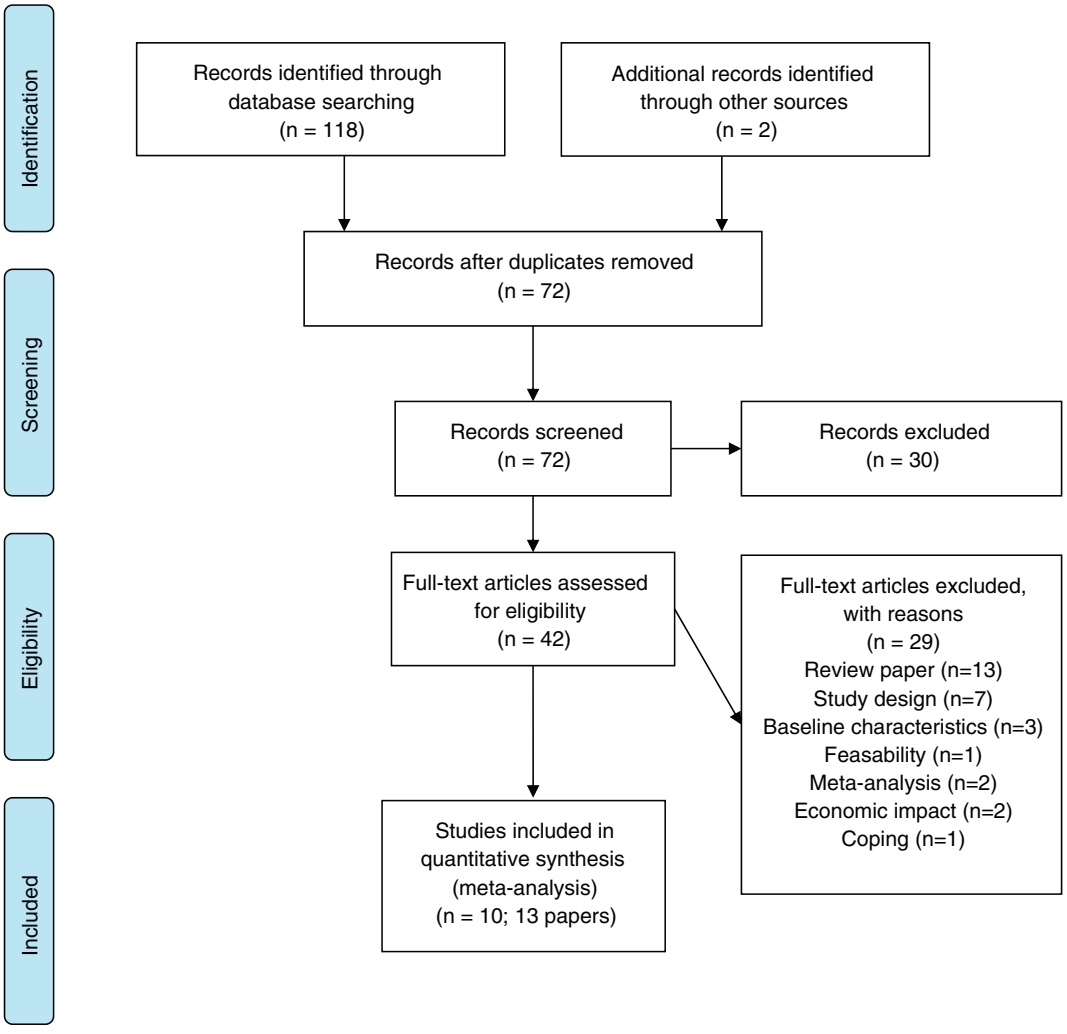

Fig. 1. Flowchart of selected studies.